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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.

EXAMINER	
ART UNIT	PAPER NUMBER

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/463,480	Applicant(s) SINGH ET AL.	
	Examiner Anne Kubelik	Art Unit 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 July 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *6-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 April 2000* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Applicant's election with traverse of Group I (claims 1-5), drawn to nucleic acids that encode LGC1, in Paper No. 15 is acknowledged. The traversal is on the ground(s) that unity of invention has been met by the claims. Applicant asserts that the three genes are linked as to form a single general inventive concept because they are all specifically expressed in generative and sperm cells and that the genes and their promoters can be used for tissue-specific expression in those cells. Furthermore, Applicant asserts that the generative and sperm cell-specific expression of these genes and their promoters constitutes a special technical feature. Lastly, Applicant asserts that the Groups are not patentably distinct.

This is not found persuasive because the prior art teaches cDNAs that would be specifically expressed in generative and sperm cells; thus, the technical feature is not special. Additionally, nucleic acids encoding different proteins are structurally distinct chemical compounds, as are different promoters structurally distinct chemical compounds; thus, they are patentably distinct.

The requirement is still deemed proper and is therefore made FINAL.

Drawings

2. The drawings are objected to for the reasons indicated on accompanying form PTO 948. Correction is required.

Specification

3. The title of the invention is not descriptive of the instant invention. A new title is required that is clearly indicative of the invention to which the claims are directed. Note that titles can be up to 500 characters long.

Claim Rejections - 35 USC § 101

4. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. Claims 1-5 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific asserted utility or a well established utility.

While the instant specification provides several utilities for the promoter of LGC1, a nonelected invention, it provides no information as to the utility of the nucleic acid encoding LSC1. As no description of the function of the LGS1 is provided, the protein can have no well-established utility. Thus, the invention has no specific asserted or well established utility.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-5 also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility

for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

8. Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for nucleic acids that encode SEQ ID NO:4, does not reasonably provide enablement for nucleic acids that encode a protein with 40% identity to SEQ ID NO:4, for nucleic acids that have 50% identity to SEQ ID NO:3, for nucleic acids that hybridize under conditions of low stringency to SEQ ID NO:3, or for derivatives of SEQ ID NO:3. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn to nucleic acids that encode a protein with 40% identity to SEQ ID NO:4, to nucleic acids that have 50% identity to SEQ ID NO:3 or that hybridize under conditions of low stringency to SEQ ID NO:3, and to nucleic acids that are derivatives of SEQ ID NO:3.

The instant specification, however, fails to provide guidance for which amino acids of SEQ ID NO:4 can be altered and to which other amino acids, and which amino acids must not be changed, to maintain the undisclosed activity of the encoded protein. The specification also fails to provide guidance for which amino acids can be deleted and which regions of the protein can tolerate insertions and still produce a functional enzyme.

It cannot be predicted by one of skill in the art that nucleic acids that hybridize to SEQ ID NO:3 or that encode proteins with homology to SEQ ID NO:4 will encode proteins with the same function as that of SEQ ID NO:4. Bowie et al (1990, Science 247:1306-10) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and

that it is the ability of the protein to fold into unique three-dimensional structures that allows it to function and carry out the instructions of the genome. The cited reference also teaches that the prediction of protein structure from sequence data and, in turn, utilizing predicted structural determinations to ascertain functional aspects of the protein, is extremely complex (pg 1306, left column). Bowie et al teach that while it is known that many amino acid substitutions are possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three-dimensional structure/function relationship, and these regions can tolerate only conservative substitutions or none at all (pg 1306, right column).

The sensitivity of proteins to alterations in even a single amino acid in a sequence is exemplified by Lazar et al (1988, Mol. Cell. Biol. 8:1247-1252), who teach that a replacement of aspartic acid at position 47 with alanine or asparagine in transforming growth factor alpha had no effect, but that replacement with serine or glutamic acid sharply reduced biological activity (see the abstract). Small changes in amino acid sequence can completely modify enzymatic function; Broun et al (1998, Science 282:1315-1317) teach that a change of four amino acids converts an oleate 12-desaturase to a hydroxylase. Thus, Lazar et al and Broun et al demonstrated that one or few amino acid substitutions could dramatically affect the biological activity and the structure-function characteristics of a protein.

Making "conservative" substitutions (*e.g.*, substituting one polar amino acid for another, or one acidic one for another) does not produce predictable results. Lazar et al (*supra*) showed that the "conservative" substitution of glutamic acid for aspartic acid at position 47 reduced biological function of transforming growth factor alpha while "nonconservative" substitutions

with alanine or asparagine had no effect (abstract). Similarly, Hill et al (1998, Biochem. Biophys. Res. Comm. 244:573-577) teach when three histidines that are maintained in ADP-glucose pyrophosphorylase across several species are substituted with the "nonconservative" amino acid glutamine, there is little effect on enzyme activity, while the substitution of one of those histidines with the "conservative" amino acid arginine drastically reduced enzyme activity (see Table 1). All these mutated proteins, however, would have much more than 40% identity to the original protein. Additionally, the nucleic acids encoding all these mutated proteins would hybridize under high stringency to the nucleic acids encoding the original protein.

Lastly, no guidance is provided as to methods of assaying the activity of the altered proteins to determine if their function is the same as that of SEQ ID NO:4. As discussed above, the function of the encoded protein is not disclosed at all.

Given the claim breath, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to develop and evaluate nucleic acids that encode a protein with 40% identity to SEQ ID NO:4, that have 50% identity to SEQ ID NO:3, that hybridize under conditions of low stringency to SEQ ID NO:3, or that are derivatives of SEQ ID NO:3.

9. Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a multitude of DNA molecules that have 50% or lower sequence similarity to SEQ ID NO:3 due to the deletion, insertion or substitution of an unspecified number of nucleotides. In contrast, the specification only describes a coding

sequence from lily that comprises SEQ ID NO:3. The specification fails to provide a description of the function of the encoded LSC1 protein and does not describe DNA molecules that encode LSC1 within the full scope of the claims.

Therefore, given the lack of written description in the specification with regard to the structural and physical characteristics of the claimed nucleic acids, and given the high level of unpredictability in this art, one skilled in the art would not have been in possession of the genus claimed at the time this application was filed.

See *University of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed. Cir. 1997):

> The name cDNA is not in itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA. Accordingly, the specification does not provide a written description of the invention ...

See Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ 2d 1016 at page 1021:

> A gene is a chemical compound, albeit a complex one, and conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials ..... Conception does not occur unless one has a mental picture of the structure of the chemical or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by its principal biological property, *e.g.*, encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property.

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 1-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention.

Dependent claims are included in all rejections.

Claims 2 and 4 are not written in proper Markush format. The claims should be in the format "selected from **the group consisting of** A, B, C and D." The words in bold are missing from the claims. See MPEP 2173.05(h).

Claim 2 is indefinite for its recitation of "fruiting plant" and "flowering plant". The metes and bounds of the claim are unclear. For example, it is not clear how fruiting plants differ from flowering plants, and how a legume, crop plant, cereal plant or grass differs from either.

Claim 3 is indefinite in its recitation of "lily or a related plant". What plants are considered related to lily is unclear, as all plants are related to lily to some extent.

Claims 4 and 5 are indefinite for including non-elected matter.

Claim 1 is indefinite for its recitation of the phrase "region facilitating its expression". The manner in which a region "facilitates" expression is unclear. Additionally, the size of the region is not specified.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 1-3 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Tuttle et al (1995, US Patent 5,477,002).

Tuttle et al teach anther-specific cDNAs expressed at different stages of anther development (Table 1). At least some of these would be specifically expressed in generative and

sperm cells. The cDNAs were isolated from tobacco, which is a crop plant, a flowering plant and a fruiting plant, and is related to lily.

14. Claims 1-3 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Baszczynski et al (1997, US Patent 5,633,438).

Baszczynski et al teach a nucleic acid, *Bnm1*, whose expression is specific to trinucleate and binucleate microspores (column 19, lines 27-51, and Fig. 2). Thus, this gene is specifically expressed in generative cells and sperm cells. The nucleic acid was isolated from *Brassica napus*, which s a crop plant, a flowering plant and a fruiting plant, and is related to lily.

15. Claims 4-5 are free of the prior, given the failure of the prior art to teach or suggest a nucleic acid that encodes a protein with 40% identity to SEQ ID NO:4.

Conclusion

16. No claim is allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (703) 308-5059. The examiner can normally be reached on Monday through Friday, 8:15 am - 4:45 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Paula K. Hutzell, can be reached on (703) 308-4310. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Anne R. Kubelik, Ph.D.
August 16, 2001

DAVID T. FOX
PRIMARY EXAMINER
GROUP 180 1638